REMARKS

This Reply, filed in response to the Office Action mailed March 21, 2008 is believed to fully address each and all issues raised in the Action. A favorable reconsideration is respectfully requested.

Claim Status

Upon entry of the accompanying Amendment, which is respectfully requested, claims 1-13 are all the claims pending in the application. Claims 11-13 are withdrawn from consideration as being directed to non-elected invention. Claims 1, 3, 5 and 6 have been amended to more clearly set forth the feature of the claimed invention. The specification is amended to describe the general name of the trademark EUDRAGIT® and present an Abstract on a separate sheet. No new matter has been introduced.

Formal Matters

Applicants thank the Examiner for approving the drawings filed on May 9, 2005.

Applicants further thank the Examiner for acknowledging claim for foreign priority and the receipt of the certified copy of the priority documents.

Response to Objection to the Specification and Claim

The Office objects to the specification because the abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). In response, the specification is amended to present a new abstract of the disclosure on a separate sheet.

Claim 4 is objected to because it allegedly contains "I" which appears to be a typographical error of numerical letter "1." Applicants carefully reviewed claim 4 in the

application as filed and respectfully submit that original claim 4 recites "based on 1 weight part of paclitaxel."

Accordingly, Applicants respectfully submit the objection to the specification become moots by the amendment and the objection to claim 4 is not sustainable, and, thus, withdrawal of the objections is respectfully requested.

Response to Rejections under 35 U.S.C. § 112

In the Office Action, claims 3, 5 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In response, claims 3, 5 and 6 are amended to correct the issues raised in the Action. In particular, un claim 3, the trade name "Eudragit" has been specified to --(meth)acrylate polymer, (meth)acrylic acid polymer and a copolymer thereof--. The "solution" in claim 5 has been amended to --obtained solution mixture--, to clearly indicate that the solution is obtained after dissolution in organic solvent. Furthermore, claim 6 has been clearly specified in conformity with the description appearing on paragraph [0027] of the specification.

Therefore, the rejection is moot by the amendment and its withdrawal is respectfully requested.

Response to Claim Rejections - 35 U.S.C. § 103

In the Office Action, claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nair (EP 0521675) in view of Patel *et al.* (U.S. Patent 6,248,363) and STN*Easy* search for paclitaxel.

Nair is relied upon to teach a method for extracting taxol from a mixture containing

taxol comprising the step of contacting the mixture with a supercritical fluid which is capable of solubilizing at least part of the contained taxol (claims 1-3). STNEasy is relied upon to teach that the term "paclitaxel" is also known by the name "taxol." The Office asserts that claims 9 of Nair teaches that the supercritical fluid includes in admixture with each other or a modifier compounds such as a haloalkane, which can be exemplified by chloroform.

The Office admits that Nair does not teach that the taxol is mixed with a surfactant or hydrophilic polymer and thus also does not teach the ratios or ranges associated with the hydrophilic polymer or surfactant; and that the organic solvent is not expressly taught as being mixed with the taxol mixture prior to contacting the supercritical fluid nor are the ratios of the organic solvents taught.

Patel is relied upon to teach the preparation of solid pharmaceutical compositions which have encapsulation coats prepared from lipophilic surfactants (col. 4, lines 4-12), wherein paclitaxel is taught as a preferred active ingredient (col. 7, lines 31-40). The Office asserts that additives such as polyvinylpyrrolidone (PVP), hydroxypropyl methylcellulose (HPMC) and hydroxyl propyl cellulose (HPC) are taught (col. 39, lines 31-37) as well as dichloromethane (col. 40, lines 36-37). The Office further asserts that Patel also teaches that several methods by which the solid compositions may be prepared by dispersion in a supercritical fluid may be used (col. 48, lines 55-61).

Applicants respectfully traverse the rejection for the following reasons:

1) Technical Features of the Claimed Invention

The claimed invention defined in pending claims 1-10 relates to a method for the preparation of a highly uniform nano-scale paclitaxel solid dispersion by a supercritical fluid process which comprises: 1) preparing a mixture of paclitaxel and a pharmaceutically acceptable additive and dissolving in a mixed organic solvent to obtain a solution mixture; 2) spraying the solution mixture of Step 1) to a supercritical fluid to bring into contact with each other to form particles of the mixture of paclitaxel and the pharmaceutically acceptable additive; 3) removing the organic solvent by washing the particles with a fresh batch of the supercritical fluid; and 4) recovering the particles prepared thereby.

The claimed method provides a highly homogeneous paclitaxel solid dispersion showing an improved solubility, which can be effectively used for the preparation of paclitaxel injection and oral preparation having a high bioavailability.

2) Summary of the Cited References

By way of review, the Nair patent, the primary reference, discloses a method for extracting taxanes such as taxol from a mixture containing such compounds, particularly from a plant or plant-derived material, comprising the step of contacting the mixture with a supercritical fluid capable of solubilizing at least part of the contained taxane (see page 2, lines 28-30 of the Nair patent). Further, the Nair patent describes that the term "extraction" means isolation and/or purification of a taxane compound, and examples of the plant or plant-derived material include plants of the genera Amentotaxus, Austrotaxus, Cephalotaxus, Pseudotaxus, Taxus and Torreya (see page 2, lines 50-51 and 55-56 of the Nair patent).

The Patel patent discloses a solid pharmaceutical composition for improved delivery of pharmaceutically active ingredients, which include a solid carrier including a substrate and an

encapsulation coat thereon (see column 4, lines 4-9 of the Patel patent). Furthermore, the Patel patent describes that the encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides; and it recites paclitaxel while enumerating a wide range of active ingredients (see column 4, lines 10-12 and column 5, line 59 of the Patel patent).

3) Comparison of the Claimed Invention with the Cited References

a) The Nair patent

Paclitaxel is sparingly soluble in water, which causes lowered bioavailability. The presently claimed invention provides a method for preparing a *highly uniform nano-scale paclitaxel solid dispersion with an improved solubility* by the supercritical fluid process.

However, the object of the Nair patent is to provide an efficient method for "isolating" taxanes such as taxol from "trees" in an environmentally safe way by minimizing the use of trees and organic solvents. In other words, the Nair patent focused on an efficient method for extracting taxol from its natural source, which can avoid using large amounts of organic solvents as well as the natural source, i.e., the slow-growing trees.

For this reason, the Nair patent is entirely silent on the process for the preparation of a solid dispersion as claimed in the subject application, while merely describing a supercritical extraction of taxol from plants. Nowhere in the Nair patent is disclosed a solid dispersion of paclitaxel

Accordingly, the subject invention relating to a specific process for the preparation of a paclitaxel solid dispersion cannot be easily derived from the Nair patent.

b) The Patel patent

The Patel patent aims to provide a solid carrier for improved delivery of active ingredients, and it provides a general composition which can be applied for any type of active ingredients rather than a specific drug like paclitaxel. Although the Patel patent mentions paclitaxel in the long list of pharmaceutical active ingredients, it neither focuses on a specific combination of paclitaxel and additives nor discloses a composition comprising paclitaxel in the working examples.

On the contrary, the claimed invention of the instant application provides a novel method for the preparation of a highly uniform nano-scale paclitaxel solid dispersion by a supercritical fluid process which comprises: 1) preparing a mixture of paclitaxel and a pharmaceutically acceptable additive and dissolving in a mixed organic solvent to obtain a solution mixture; 2) spraying the solution mixture of Step 1) to a supercritical fluid to bring into contact with each other to form particles of the mixture of paclitaxel and the pharmaceutically acceptable additive; 3) removing the organic solvent by washing the particles with a fresh batch of the supercritical fluid; and 4) recovering the particles prepared thereby. The paclitaxel solid dispersion prepared by the above method has a structure totally different from the solid carrier having an encapsulation coat as taught by the Patel patent.

c) A combination of the cited references

Applicants respectfully submit that there is no motivation to combine the Nair patent and the Patel patent. They do not share any technical problem to solve. The Nair patent intends to provide a method for isolating taxol from plants while the Patel patent aims to provide a solid carrier for improved delivery of active ingredients, there is no common feature between the

references, which can provide a motivation for those skilled in the art to combine the two inventions.

Even if they are combined together, the unique process for the preparation of paclitaxel solid dispersion of the claimed invention cannot be conceived therefrom. Furthermore, the claimed method provides a remarkably improved solubility of the paclitaxel solid dispersion prepared by the subject process (see Table 25 of the subject specification). Specifically, the solubilities of the paclitaxel solid dispersions prepared by the supercritical fluid process of the subject invention are remarkably higher (about 3,000 times) than that of the solid dispersion prepared using liquid carbon dioxide or a conventional paclitaxel powder. In contrast, although the compositions are not for paclitaxel, the dissolution ratios of the glyburide composition of Example 2 and the progesterone composition of Example 3 of the Patel patent showed merely 2 to 3 times than that of the pure bulk drug (see Figures 1, 2A and 2B of the Patel patent).

As described above, it is believed that the claimed methods of the present application and the teachings of the cited references are clearly different, and the unique feature of the present invention as well as the unexpected remarkable effects arising therefrom are not taught, suggested or disclosed by the cited references, even if they are combined.

Accordingly, the present invention defined in claims 1-10 is clearly patentable and unobvious over the cited references, and it is respectfully submitted that the 103 rejections of claims 1-10 should be withdrawn.

CONCLUSION

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. **If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at telephone number 202-775-7588.**

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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